Claims

1. Compounds of the general formula (I) - wherein

R^1 means a nitrogen-containing aromatic moiety consisting of one or two aromatic rings, preferably a pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, imidazolyl, pirazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, benzimidazolyl, indazolyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl or benzisoxazolyl, tetrazolyl, triazinyl ring; which is, in a given case, independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl groups, C1-4 alkoxy groups, halogen atom, trihalogenomethyl group, methylthio group, nitro group, cyano group, amino group or phenyl group; or

- thienyl, furyl or benzyl group; or
- p-toluenesulfonyl group; or
- acyl group of formula R_{1a}-CO, wherein R_{1a} means C1-4 alkyl group, phenyl group; phenyl, pyridyl or phenylethenyl group substituted with one or more alkyl- and/or alkoxy- or nitro-group or halogen atom; phenylethenyl or phenylethyl group substituted with alkylene-dioxy group; piperidin-1-yl, 4-methylpiperazin-1-yl, pyrrolidin-1-yl group,

B stands for

- a group of formula (1) or (2) or (3) or (4) or (5) or (6) or (7);

R^2 stands for hydrogen atom or fluorine atom;

R^3 stands for fluorine atom -

and salts, isomers, tautomers, solvates and hydrates thereof.

2. Compounds of claim 1of the general formula (I) - wherein

R^1 means a nitrogen-containing aromatic moiety consisting of one or two aromatic rings, preferably a pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, imidazolyl, pirazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, benzimidazolyl, indazolyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl or benzisoxazolyl ring; which is, in a given case, independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl groups, C1-4 alkoxy groups, halogen atom, trihalogenomethyl group, methylthio group, nitro group, cyano group; or

- thienyl or furyl group; or

- p-toluenesulfonyl group; or

- acyl group of formula R_{1a}-CO, wherein R_{1a} means C1-4 alkyl group, phenyl group; phenyl, pyridyl or phenylethenyl group substituted with one or more alkyl- and/or alkoxy- or nitro-group or halogen atom; phenylethenyl or phenylethyl group substituted with alkylene-dioxy group; piperidin-1-yl, 4-methylpiperazin-1-yl, pyrrolidin-1-yl group,

B stands for

- a group of formula (1) or (2) or (3) or (4) or (5) or (6) or (7);

R^2 stands for hydrogen atom or fluorine atom;

R^3 stands for fluorine atom -

and salts, isomers, tautomers, solvates and hydrates thereof.

3. Compounds of claim 2 of the general formula (I) - wherein

R^1 means a nitrogen-containing aromatic moiety consisting of one or two aromatic rings, preferably a pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, imidazolyl, pirazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, benzimidazolyl, indazolyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl or benzisoxazolyl ring; which is, in a given case, independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl groups, C1-4 alkoxy groups, halogen atom, trihalogenomethyl group, methylthio group, nitro group, cyano group; or

- thienyl or furyl group; or

- p-toluenesulfonyl group; or

- acyl group of formula R_{1a}-CO, wherein R_{1a} means C1-4 alkyl group, phenyl group; phenyl, pyridyl or phenylethenyl group substituted with one or more alkyl- and/or alkoxy- or nitro-group or halogen atom; phenylethenyl or phenylethyl group substituted with alkylene-dioxy group; piperidin-1-yl, 4-methylpiperazin-1-yl, pyrrolidin-1-yl group,

B stands for

- a group of formula (1);

R^2 stands for hydrogen atom or fluorine atom;

R^3 stands for fluorine atom -

and salts, isomers, tautomers, solvates and hydrates thereof.

4. Compounds of claim 2 of the general formula (I) - wherein

R^1 means a nitrogen-containing aromatic moiety consisting of one or two aromatic rings, preferably a pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, imidazolyl, pirazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, benzimidazolyl, indazolyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl or benzisoxazolyl ring; which is, in a given case, independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl groups, C1-4 alkoxy groups, halogen atom, trihalogenomethyl group, methylthio group, nitro group, cyano group; or

a thienyl or furyl group; or

a p-toluenesulfonyl group; or

an acyl group of formula R_{1a}-CO, wherein R_{1a} means C1-4 alkyl group, phenyl group; phenyl, pyridyl or phenylethenyl group substituted with one or more alkyl- and/or alkoxy- or nitro-group or halogen atom; phenylethenyl or phenylethyl group substituted with alkylene-dioxy group; piperidin-1-yl, 4-methylpiperazin-1-yl, pyrrolidin-1-yl group,

B stands for

- a group of formula (2);

R^2 stands for hydrogen atom or fluorine atom;

R^3 stands for fluorine atom -

and salts, isomers, tautomers, solvates and hydrates thereof.

5. Compounds of claim 2 of the general formula (I) - wherein

R^1 means a nitrogen-containing aromatic moiety consisting of one or two aromatic rings, preferably a pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, imidazolyl, pirazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, benzimidazolyl, indazolyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl or benzisoxazolyl ring; which is, in a given case, independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl groups, C1-4 alkoxy groups, halogen atom, trihalogenomethyl group, methylthio group, nitro group, cyano group; or

a thienyl or furyl group; or

a p-toluenesulfonyl group; or

an acyl group of formula R_{1a}-CO, wherein R_{1a} means C1-4 alkyl group, phenyl group; phenyl, pyridyl or phenylethenyl group substituted with one or more alkyl- and/or alkoxy-

or nitro-group or halogen atom; phenylethenyl or phenylethyl group substituted with alkylene-dioxy group; piperidin-1-yl, 4-methylpiperazin-1-yl, pyrrolidin-1-yl group,

B stands for

- a group of formula (3);

R^2 stands for hydrogen atom or fluorine atom;

R^3 stands for fluorine atom -

and salts, isomers, tautomers, solvates and hydrates thereof.

6. Compounds of claim 2 of the general formula (I) wherein

R^1 means a nitrogen-containing aromatic moiety consisting of one or two aromatic rings, preferably a pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, imidazolyl, pirazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, benzimidazolyl, indazolyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl or benzisoxazolyl ring; which is, in a given case, independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl groups, C1-4 alkoxy groups, halogen atom, trihalogenomethyl group, methylthio group, nitro group, cyano group; or

a thienyl or furyl group; or

a p-toluenesulfonyl group; or

an acyl group of formula R_{1a}-CO, wherein R_{1a} means C1-4 alkyl group, phenyl group; phenyl, pyridyl or phenylethenyl group substituted with one or more alkyl- and/or alkoxy- or nitro-group or halogen atom; phenylethenyl or phenylethyl group substituted with alkylene-dioxy group; piperidin-1-yl, 4-methylpiperazin-1-yl, pyrrolidin-1-yl group,

B stands for

- a group of formula (4) or (5);

R^2 stands for hydrogen atom or fluorine atom;

R^3 stands for fluorine atom -

and salts, isomers, tautomers, solvates and hydrates thereof.

7. Compounds of claim 2 of the general formula (I) - wherein

R^1 means a nitrogen-containing aromatic moiety consisting of one or two aromatic rings, preferably a pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, imidazolyl, pirazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, benzimidazolyl, indazolyl, benzothiazolyl,

benzisothiazolyl, benzoxazolyl or benzisoxazolyl ring; which is, in a given case, independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl groups, C1-4 alkoxy groups, halogen atom, trihalogenomethyl group, methylthio group, nitro group, cyano group; or

a thienyl or furyl group; or

a p-toluenesulfonyl group; or

an acyl group of formula R_{1a}-CO, wherein R_{1a} means C1-4 alkyl group, phenyl group; phenyl, pyridyl or phenylethenyl group substituted with one or more alkyl- and/or alkoxy- or nitro-group or halogen atom; phenylethenyl or phenylethyl group substituted with alkylene-dioxy group; piperidin-1-yl, 4-methylpiperazin-1-yl, pyrrolidin-1-yl group,

B stands for

- a group of formula (6) or (7);

R^2 stands for hydrogen atom or fluorine atom;

R^3 stands for fluorine atom -

and salts, isomers, tautomers, solvates and hydrates thereof.

8. Compounds of claims 2 and 3 of the general formula (I) - wherein

R^1 means 2-pyrimidinyl, 2-pyrazinyl, chloro- and cyano-substituted pyridazinyl, cyano-substituted 2-pyridinyl; B stands for a group of formula (1); R^2 and R^3 stand for fluorine atom.

9. Compounds of claims 2 and 4 of the general formula (I) - wherein

R^1 means 2-pyrimidinyl, 2-pyrazinyl, chloro- and cyano-substituted pyridazinyl, cyano-substituted 2-pyridinyl; B stands for a group of formula (2); R^2 and R^3 stand for fluorine atom.

10. Compounds of claims 2 and 5 of the general formula (I) - wherein

R^1 means 2-pyrimidinyl, 2-pyrazinyl, chloro- and cyano-substituted pyridazinyl, cyano-substituted 2-pyridinyl; B stands for a group of formula (3); R^2 and R^3 stand for fluorine atom.

11. Compounds of claims 2 and 6 of the general formula (I) - wherein

R^1 means 2-pyrimidinyl, 2-pyrazinyl, chloro- and cyano-substituted pyridazinyl, cyano-substituted 2-pyridinyl; B stands for a group of formula (4) or (5); R^2 and R^3 stand for fluorine atom.

12. Compounds of claims 2 and 7 of the general formula (I) - wherein
R^1 means 2-pyrimidinyl, 2-pyrazinyl, chloro- and cyano-substituted pyridazinyl, cyano-substituted 2-pyridinyl; B stands for a group of formula (6) or (7); R^2 and R^3 stand for fluorine atom.

13. (2*S*)-4,4-difluoro-1-(2-{[8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl] *exo*-amino}acetyl)-2-pyrrolidine carbonitrile;

14. (2*S*,4*S*)-4-fluoro-1-(2-{[8-(2-pyrazinyl)-8-azabicyclo-[3.2.1]-oct-3-yl] *exo*-amino}acetyl)-2-pyrrolidinecarbonitrile;

15. (2*S*)-4,4-Difluoro-1-(2-{[1-(2-pyrazinyl)piperidin-4-yl]amino}acetyl)-2-pyrrolidine carbonitrile;

16. (2*S*)-4,4-Difluoro-1-(2-{[1-(5-cyanopyridin-2-yl)piperidin-4-yl]amino} acetyl)-2-pyrrolidine carbonitrile;

17. (2*S*)-4,4-Difluoro-1-(2-{[1-(6-chloropyridazin-3-yl)piperidin-4-yl] amino}acetyl)-2-pyrrolidine carbonitrile;

18. (2*S*)-4,4-Difluoro-1-(2-{[1-(6-cyanopyridazin-3-yl)piperidin-4-yl] amino}acetyl)-2-pyrrolidine carbonitrile;

19. Pharmaceutical formulation comprising a compound of the general formula (I) according to claims 1 to 18 or salts, isomers, tautomers, solvates, hydrates thereof.

20. Process for the preparation of the compounds of the general formula (I) - wherein the meanings of R^1, B, R^2 and R^3 are the same as defined in Claims 1 to 12 – characterised in that, a compound of the general formula (II) – wherein the meanings of R^1 and B are as defined above – is reacted with a compound of the general formula (III) – wherein the

meanings of R^2 and R^3 are as defined above – and the resulting compound of the general formula (I) or its salt is isolated from the reaction mixture.

21. Use of a compound of the general formula (I) -wherein the meanings of R^1, B, R^2 and R^3 are the same as defined in Claims 1 to 12 – for the preparation of a pharmaceutical formulation which are suitable to inhibit the activity of DPP-IV enzyme, and intended for the treatment and the prevention of diseases related with the DPP-IV enzyme activity.

22. Use of a compound of the general formula (I) -wherein the meanings of R^1, B, R^2 and R^3 are the same as defined in Claims 1 to 12 – for the preparation of a pharmaceutical formulation which are suitable to inhibit the activity of DPP-IV enzyme, and intended for the treatment and the prevention of diabetes.

23. Compounds of the general formula (II) – wherein the meanings of R^1 and B are as defined in claims 1 to 12 – and their isomers and salts.

24. Compounds of the general formula (III) –wherein the meanings of R^2 and R^3 are as defined in claims 1 to 12– and their isomers.

25. Compounds of the general formula (V) - wherein the meanings of R^1 and B are as defined in claims 1 to 12, Y stands for acetyl or *tert*-butoxycarbonyl group - and their isomers and salts.

26. Compounds of the general formula (VII) – wherein the meanings of R^2 and R^3 are as defined in claims 1 to 12 - and their isomers.

27. Compounds of the general formula (VIII) – wherein the meanings of R^2 and R^3 are as defined in claims 1 to 12 - and their isomers and salts.

28. Compounds of the general formula (IX)– wherein the meanings of R^2 and R^3 are as defined in claims 1 to 12- and their isomers.

29. Use of compounds of the general formula (II), (III), (V), (VII), (VIII) and (IX) according to claims 22 to 27 for the preparation of compounds of the general formula (I) defined in claims 1 to 18.